15 de noviembre de 2022

ISQ-201: Lead compound from a new family of small molecules “steronitrones”

Youness Ouahid

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ISQUAEMIA BIOTECH

The company

New drugs for vascular and Central Nervous System pathologies, with a first line of development in ACUTE ISCHEMIC STROKE (AIS).

isquaemia BIOTECH

NEUROVASCULAR DRUG DEVELOPMENT COMPANY

European Commission
SEAL OF EXCELLENCE

PYME INNOVADORA
Válido hasta el 12 de marzo de 2021
GOBIERNO DE ESPAÑA · MINISTERIO DE ECONOMÍA, INDUSTRIA Y COMPETITIVIDAD

Fundación para la Investigación Biomédica del Hospital Universitario Ramón y Cajal

CSIC
Consejo Superior de Investigaciones Científicas

THE PRODUCT: ISQ-201

Target Indications

MAIN INDICATION

Acute Ischemic Stroke (AIS).

ISQ-201 reduces neurological damage and therefore the comorbidity caused by this pathology, reducing disability, and increasing the quality of life of patients. The drug candidate ISQ-201 has successfully completed the GLP preclinical phase and is facing GMP regulatory phase.

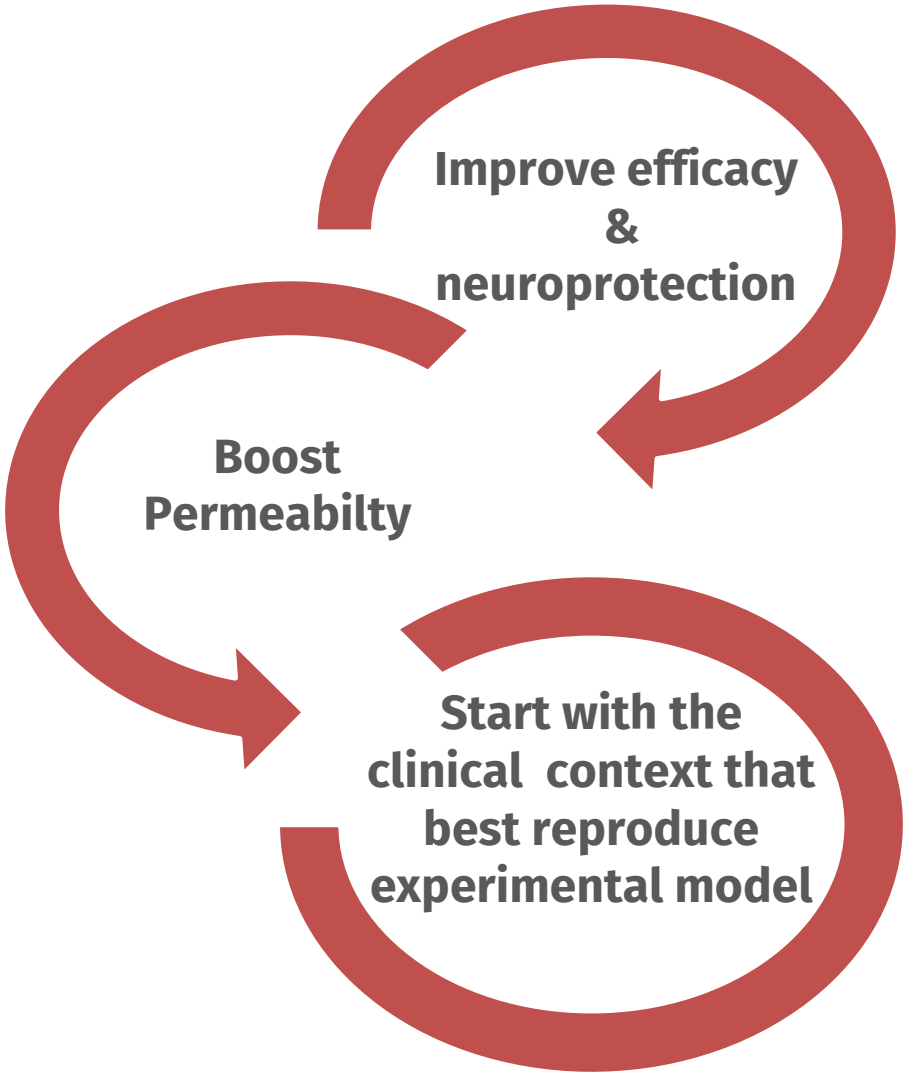
OTHER INDICATIONS

Permanent ischemia, CPR & ALS.

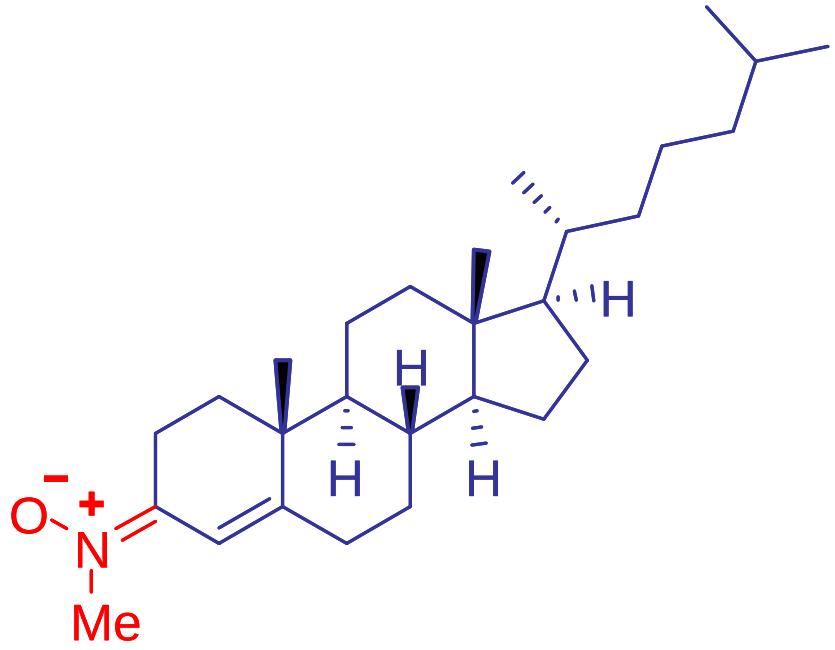
ISQUAEMIA plans to expand the clinical use of **ISQ-201** for other applications such as **permanent ischemia**. In addition, the preliminary results also indicate its potential use in other neurological pathologies, such as **Amyotrophic Lateral Sclerosis (ALS)**.

THE PRODUCT: ISQ-201

Differential features facing the market



ISQ-201: Nitrone (antioxidant activity) + Cholestene steroid (delivery)



Thrombectomy as clinical first target to ensure ISQ-201 action in (controlled) reperfusion

THE PRODUCT

Innovative mechanisms of action

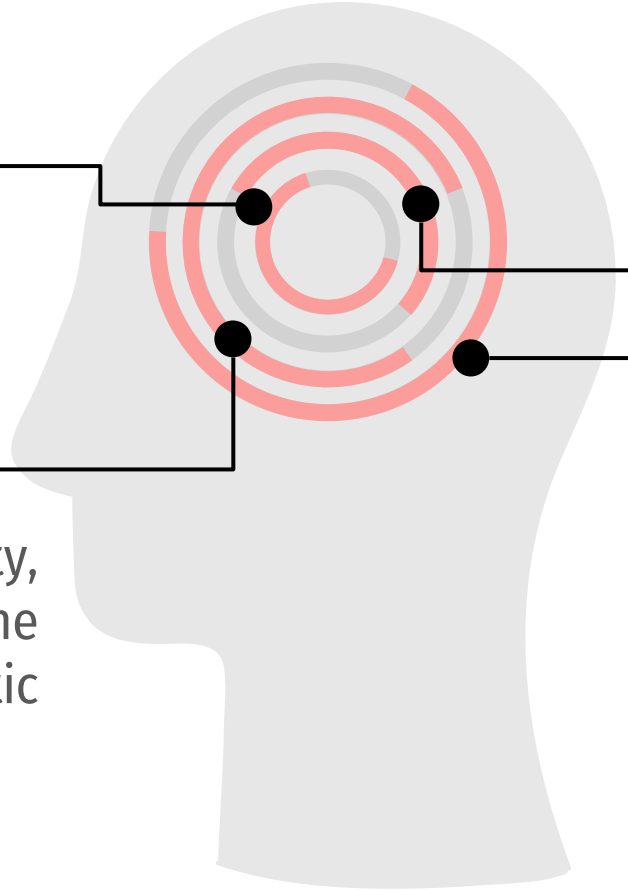
Isquaemia is developing a **new neuroprotective drug** for acute ischemic stroke treatment, which acts rapidly in the penumbra zone.

Neuroprotection

Infarct size reduction and cognitive and motor improvement

Cell permeability

High blood-brain barrier permeability, enhancing the bioavailability of the drug and improving its therapeutic activity.



Neuroprotective

Decreased neuronal death and apoptosis

Antioxidant

Oxidative stress reduction: antioxidant agent and activation of the cellular antioxidant response

Maria I. Ayuso et al. CholesteroNitrones for Stroke. J. Med. Chem. 2015, 58, 16, 6704–6709.

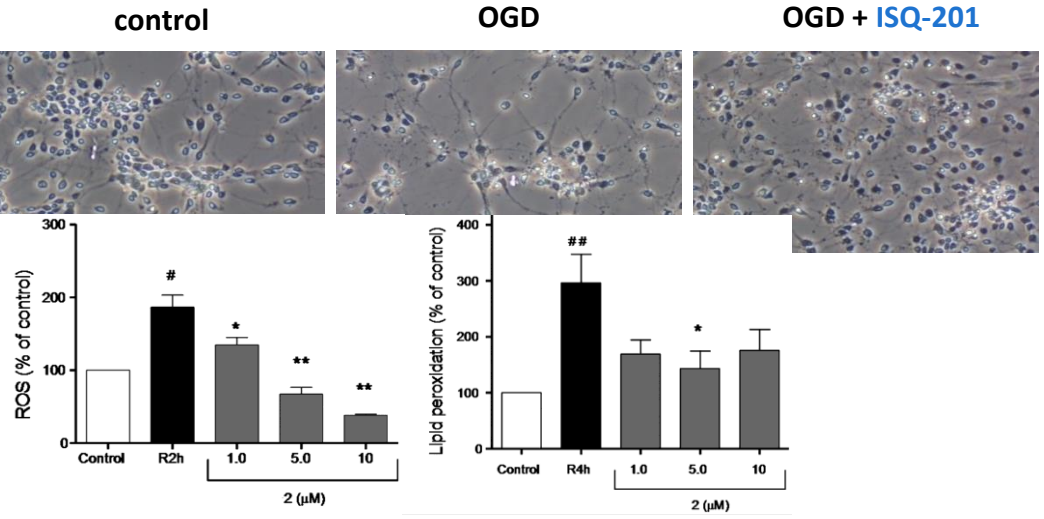
THE PRODUCT

Current status of development

Drug discovery → Preclinical Assays → GMP Regulatory phase → Clinical Trials

In Vitro Studies ✓

Oxygen–Glucose Deprivation (OGD)
Primary neuronal cultures.
Efficacy, Toxicity & MoA.



Journal of Medicinal Chemistry

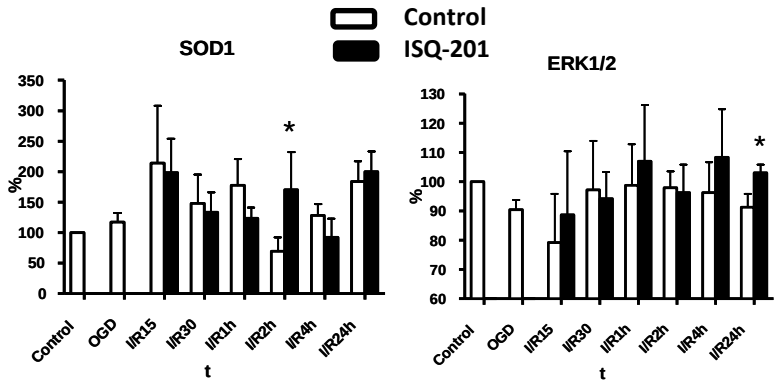
Brief Article

pubs.acs.org/jmc

CholesteroNitrones for Stroke

Maria I. Ayuso,[†] Mourad Chioua,[*,‡] Emma Martínez-Alonso,[†] Elena Soriano,[§] Joan Montaner,[∥] Jaime Masjuán,[⊥] Dimitra J. Hadjipavlou-Litina,[#] José Marco-Contelles,[*,‡] and Alberto Alcázar[*,†]

Neuroprotective effect & Decreased level of lipid peroxidation and ROS signal translation in neurons after OGD.



THE PRODUCT

Current status of development

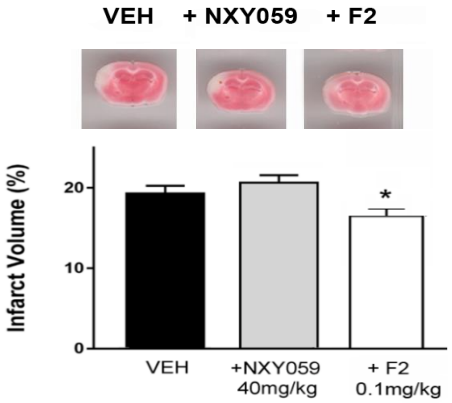
isquaemia BIOTECH

Drug discovery → Preclinical Assays → GMP Regulatory phase → Clinical Trials

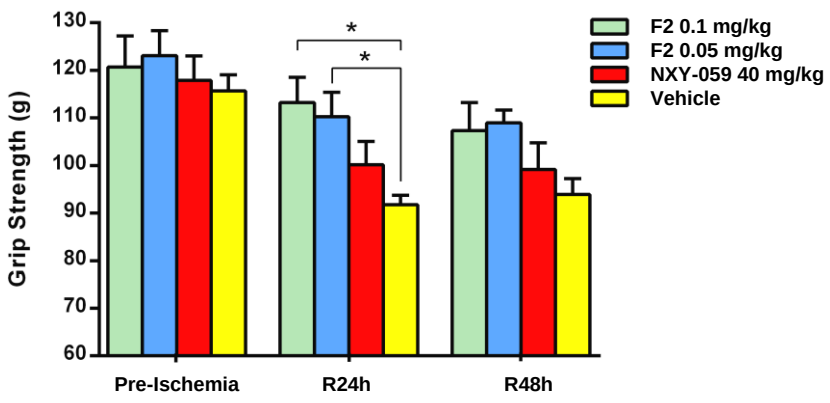
In Vivo Studies ✓

Focal cerebral ischemia model.
Transient global cerebral ischemia model.

•Infarct size assessment



•Neurological deficit assessment



antioxidants

MDPI

Article

Characterization of a CholesteroNitrone (ISQ-201), a Novel Drug Candidate for the Treatment of Ischemic Stroke

Emma Martínez-Alonso [1], Alejandro Escobar-Peso [1], Maria I. Ayuso [2], Rafael Gonzalo-Gobernado [2], Mourad Chioua [3], Juan J. Montoya [4], Joan Montaner [2,5], Israel Fernández [6,*], José Marco-Contelles [3] and Alberto Alcázar [1,*]

- ✓ *Decreased neuronal death in regions vulnerable to the ischemia-reperfusion damage — hippocampus and cortex. Significant reduction of infarct size.*
- ✓ *Improvement of long-term cognitive impairment and functional motor deficit*

THE PRODUCT

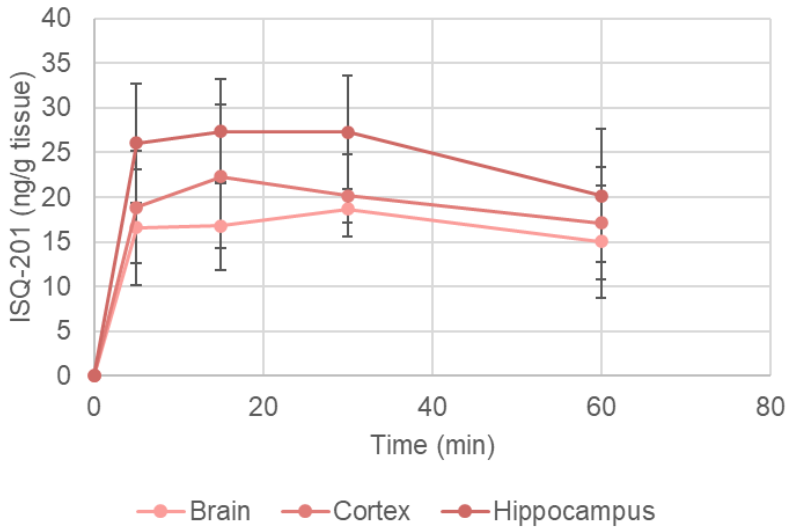
Current status of development

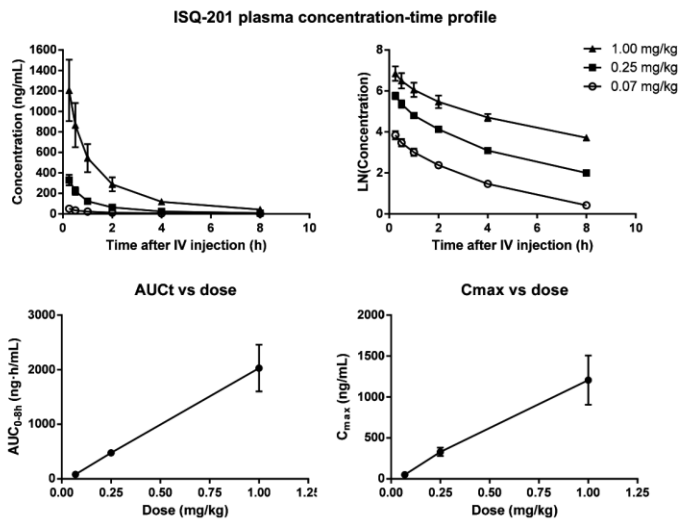
Non toxic & non mutagenic
Non Haemolytic Activity

Drug discovery → Preclinical Assays → GMP Regulatory phase → Clinical Trials

GLP preclinical phase ✔

PHARMACOKINETICS, TOXICITY & BIODISTRIBUTION





antioxidants — MDPI

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Vall d'Hebron Institut de Recerca

vivotecnia researching for you

IBIS INSTITUTODEBIOMEDICINADESEVILLA

eurofins

Synthelia Organics

amylgen IN VIVO DRUG DISCOVERY

admescope A SYMERES COMPANY

THE PRODUCT

Current status of development

Drug discovery → Preclinical Assays → GMP Regulatory phase → Clinical Trials

TEMPORARY THERAPEUTIC WINDOW (AFTER REPERFUSION)	PROVEN EFFICACY FROM 0 TO 6 HOURS AFTER REPERFUSION
THERAPEUTIC SAFETY WINDOW (TOXICOLOGICAL)	0.05 MG/KG THERAPEUTIC DOSE
	TESTED UP TO 1 MG/KG WITHOUT TOXICITY
AVERAGE LIFETIME	90 MINUTES
ADMINISTRATION	SINGLE INTRAVENOUS INJECTION
PREPARATION STABILITY	7 HOURS
BBB PERMEABILTY	8,3/1 [Brain/Blood]
OTHERS	NON TOXICITY (HAEMOLITIC; GENOTOXIC; MUTAGENIC; PRO-MUTAGENIC; CARDIOTOXIC, CHRONIC...)

NITRONE	logBB	[Brain]/[Blood]
ISQ-201	0.92	8.3/1
NXY-059	-1.9	1/79

HEMATOENCEPHALIC PERMEABILITY OF ISQ-201
659 TIMES MORE THAN NXY-059

THE PRODUCT

IPR protection

Isquaemia's new drug is protected under several patent families.

PCT/ES2014/070421: *Steroidal nitrones for the treatment and prevention of AIS, Alzheimer, Parkinson diseases and Amyotrophic Lateral Sclerosis.*

Lead Compound - CNS

PCT/EP2019/077525: *Quinolylnitrones for the treatment and prevention of a cerebral stroke or ischaemia.*

Backup Compound - AIS

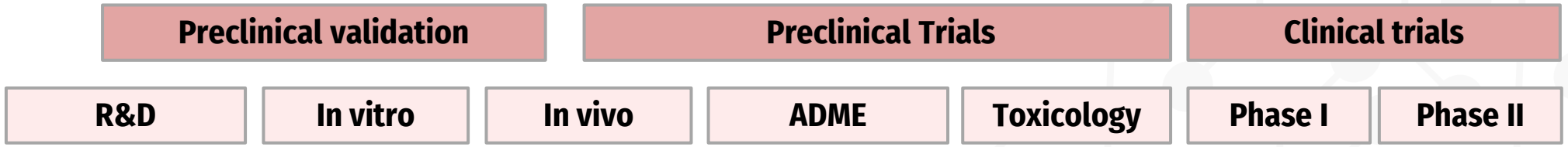
PCT/EP2021/055653: *"Steroidal nitrone for the treatment and/or Prevention of a cerebral stroke or ischaemia.*

New Stroke Indication

THE PRODUCT

Pipeline

Isquaemia is considering **additional lines of preclinical and clinical development** with the aim of broadening the range of patients potentially treatable with ISQ-201, both in IIA (hospital and emergency treatment) and in other neurological pathologies with oxidative damage. In addition, the company has a **second drug candidate, ISQ-202**, which has also shown great potential in preclinical stroke models.



Acute Ischemic Stroke

ISQ-201A — Acute Ischemic Stroke

ISQ-202 — Acute Ischemic Stroke

Other indications:

Chronic Ischemic Stroke.
ALS, Alzheimer, Parkinson.

ISQ-201B

THE PRODUCT

Pitfalls & Risks to be considered

Risks	Likelihood	Impact	Mitigations
GMP Synthesis Batch Issues	Rare	Low	Identification of outsourcing activities. Tech Transfer activity from Lab. Synthesis already available
Preclinical Final Toxicity Test Failure	Unlikely	High	Repeated dose toxicity assay (up to 20-fold cc) were negative
Failure (Toxicity vs Activity) of Human Clinical Trials	Possible	Very High	We have both backup compounds and a wide range for administration dose adjustments
Low BBB permeability in humans	Unlikely	Medium	The steroid structure of ISQ-201 ensures high permeability to BBB, proved in silico and in vivo

PARTNERING OPPORTUNITIES

Open to different proposals: from Licencing, M&A or Joint-Venture to milestones & hits driven agreements.

Currently we are negotiating an M&A with a US Clinical Trial phase company with whom we have synergic pipeline (Stroke)

Fundraising campaign (2-3,5M€) open to ensure FIH development.
Due Diligence and evaluation done by Ineo Corporate

15 de noviembre de 2022

isquaemia BIOTECH

ISQ-201: Lead compound from a new family of small molecules “steronitrones”

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